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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,151	ZHONG ET AL.	
	Examiner	Art Unit	
	RACHAEL WELTER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 14-37* is/are pending in the application.

4a) Of the above claim(s) *22-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 7/22/11 has been entered.

Claim Status

Claims 1-8 and 14-37 are pending. Claims 1-8 and 14-21 are drawn to the elected invention. Claims 22-37 are withdrawn. Claims 9-13 and 38-39 are cancelled.

Withdrawn Rejections

The rejection of claims 1-6, 11-12, 20-21 under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689; already made of record) is withdrawn in light of applicant's amendments.

The rejection of claims 9-10, 13, 19 under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Ramsack et al. (US Patent 6,667,061) is withdrawn in light of applicant's amendments.

The rejection of claims 7-8 under 103(a) as being unpatentable over Escandon et al (US Patent Application Pub. No. 2003/0092689), in view of Ramsack et al. (US Patent 6,667,061), in further view of Lund (US Patent 3,869,546) is withdrawn in light of applicant's amendments.

The rejection of claims 14, 16-18 under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Glajch et al. (US Patent 5,147,631; already made of record) is withdrawn in light of applicant's amendments.

The rejection of claim 15 under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Lauffer et al. (US Patent 7,175,829) is withdrawn in light of applicant's amendments.

The rejection of claims 38-39 under 103(a) as being unpatentable over Escandon et al. (US Patent Application Pub. No. 2003/0092689), in view of Cochrum (US Patent 5,614,204) is withdrawn in light of applicant's amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 14-16, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carpenter et al (US 2003/0044354).

Carpenter et al teach formulations comprising gas microsphere liposomes suspended in a medium, which is used in ultrasound imaging (abstract). The formulations are sterile aqueous solutions containing mixtures of glycerol, liquid polyethylene glycols, ethanol, or other suitable parenteral diluents that can be administered via injection (paragraphs 0106-0107). Example 1 of Carpenter et al is directed to a saline glycerol solution comprising 10 wt.% propylene glycol and 9 wt.%

sodium chloride (paragraph 0099; paragraph 0114). The formulations can comprise diagnostic agents such as X-ray and MRI contrast agents (paragraph 0066).

Although Carpenter et al suggest the instant viscosity adjusting agent, polyethylene glycol, it is not immediately envisaged and therefore the instant rejection is made under obviousness.

However, it would have been obvious to an artisan of ordinary skill at the time the invention was made to look at the guidance provided by Carpenter et al and incorporate polyethylene glycol in its formulation as a diluent. One would have been motivated to do so since Carpenter et al suggest the use of polyethylene glycol as a suitable alternative among diluents. Furthermore, it is within the skill of an artisan to select a given diluent depending on the desired use, fluidity, and stability of the formulation.

Regarding the limitations wherein the chemical ablation agent and viscosity adjusting agent are in amounts effective to cause tissue necrosis and render the formulation highly viscous, it is noted that the instant specification teaches amounts of chemical ablation agent and viscosity adjusting agent in amounts of 5-35 wt.% and 1-20 wt.% respectively (see instant specification paragraphs 0025 and 0028). Thus, since Carpenter et al teach amounts of viscosity adjusting agent or diluent(10% propylene glycol) and chemical ablation agent (9 % sodium chloride) that fall within the ranges cited in the specification, it is the examiner's position that these amounts are effective to cause tissue necrosis and render a formulation highly viscous.

Regarding the limitations directed to a plurality of viscosity adjusting agents and a plurality of ablation agents, the examiner reminds applicant that it is obvious to add

more than one equivalent ingredient for the same intended purpose. It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven,* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06). As such, one would have a reasonable expectation of success to add both a plurality of viscosity adjusting agents and a plurality of ablation agents in the formulations of Carpenter et al.

Claims 7-8 are rejected under 103(a) as being unpatentable over Carpenter et al (US 2003/0044354) as applied to claims 1-6, 14-16, and 19-21 above and in further view of Lund (US Patent 3,869,546).

The disclosure of Carpenter et al is discussed above.

Carpenter et al do not explicitly teach the instant viscosity range from 5,000-100,000 cps and more specifically, 10,000-50,000 cps.

Lund teaches improved injectable mixtures containing biologics, a polymer, and an electrolyte having a viscosity of about 500 to about 50,000 cps, depending on the relative concentration of the polymer (col. 6, lines 36-46). Lund state that the viscosity of polymer-electrolyte adjuvant solutions should generally be about several hundred to a few thousand centipoise for ease of passing through hypodermic needles (col. 4, lines 39-42).

Therefore, it would have been obvious to an ordinary skilled artisan at the time the invention was made to manipulate and optimize the injectability of Carpenter's formulation. One would have been motivated to do so because Lund teaches that viscosity of formulations that are injected via hypodermic needles should be about 500 to about 50,000 cps, depending on the relative concentration of the polymer (col. 6, lines 36-46). Hence, one would reasonably expect to successfully manipulate the viscosity of Carpenter's formulation in order to enhance its injectability.

Claims 17-18 are rejected under 103(a) as being unpatentable over Carpenter et al (US 2003/0044354) as applied to claims 1-6, 14-16, and 19-21 above and in further view of Glajch et al (US Patent 5,147,631).

The disclosure of Carpenter et al is discussed above.

Carpenter et al do not teach an ultrasonic imaging contrast agent comprising a plurality of solid particles, including calcium carbonate particles, hydroxyapatite particles, silica particles, etc.

Glajch et al teach ultrasound contrast agents comprising porous particles of an inorganic material having an average particle diameter of about 0.05 to 500 microns and containing entrapped gas or liquid; the inorganic material includes monomeric and polymeric forms of one or more of the following: borates, aluminas, carbonates, silicates, silicas, aluminosilicates, phosphates, and organic or inorganic cationic salts thereof (column 2, lines 11-27).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to add an ultrasonic imaging contrast agent comprising a plurality of solid particles. One would have been motivated to do so since Glajch et al teach that the particles can be administered parenterally and are conventionally used to enhance the ultrasound image of a tissue or organ system of a person. Additionally, one would have been motivated to do so since Glajch et al teach that the inorganic particles of the invention have the advantages of good mechanical stability and rigidity, which are important attributes lacking in other materials used as ultrasound contrast agents (see column 4, lines 51-66).

Response to Arguments

Applicant's arguments with respect to the Examiner's Answer mailed 5/24/11 have been considered but are moot in view of the new ground(s) of rejection above. The rejections are no longer rejected over Escandon and applicant is directed to the new primary reference, Carpenter.

Conclusion

Claims 1-8 and 14-21 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RACHAEL WELTER whose telephone number is (571)270-5237. The examiner can normally be reached 7:30-5:00 Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

REW

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611